Citation:

Oken E, Radesky JS, Wright RO, Bellinger DC, Amarasiriwardena CJ, Kleinman KP, Hu H, Gillman MW. Maternal fish intake during pregnancy, blood mercury levels, and child cognition at age 3 years in a US cohort. *Am J Epidemiol.* 2008 May 15;167(10):1171-81. Epub 2008 Mar 18.

PubMed ID: 18353804

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To study associations of maternal second-trimester fish intake and erythrocyte mercury levels with children's scores on the Peabody Picture Vocabulary Test and the Wide Range Assessment of Visual Motor Abilities at age 3 years.

Inclusion Criteria:

- Subjects were participants in Project Viva, a prospective prebirth cohort study in Massachusetts.
- Criteria included completing a prenatal dietary questionnaire, information on maternal fish intake, stored maternal blood samples, and cognitive test results for children aged 3 years.

Exclusion Criteria:

- Lack of information on maternal fish intake
- Lack of stored blood samples
- No testing information for the children.

Description of Study Protocol:

Recruitment Subjects were participants in Project Viva, a prospective prebirth cohort study in Massachusetts.

Design - Prospective, prebirth cohort study of 341 mother-child pairs.

Blinding used (if applicable) not applicable

Intervention (if applicable) not applicable

Statistical Analysis

- t-tests and chi-square analysis, Spearman's correlation and simple linear regression models were used
- Multivariate linear regression was used to examine the associations of participant characteristics and exposures of interest with child cognitive test scores.
- Fish intake and mercury levels were also classified and analyzed.
- Dietary and blood levels of DHA + EPA and maternal blood mercury levels were analyzed.
- Multiple covariates were taken into consideration for the statistical calculations.

Data Collection Summary:

Timing of Measurements

- Maternal second-trimester fish intake and erythrocyte mercury levels.
- The child's Peabody Vocabulary Test and the Wide Range Assessment of Visual Motor Abilities was taken at 3 years of age.

Dependent Variables

- Child's cognition test scores (Peabody Vocabulary Test and the Wide Range Assessment of Visual Motor Abilities)

Independent Variables

- Maternal fish intake - semiquantitative food frequency questionnaire
- Red blood cell mercury levels - blood samples were taken during the 2nd trimester visit. The samples were treated with EDTA, and centrifuged. The plasma was separated from the erythrocytes.
- Dietary fatty acids. Summed intake from all foods and supplements. Estimated DHA + EPA from fish. The Harvard nutrient database was used to make these determinations.

Control Variables - none listed. Several covariates (from interviews and questionnaires) were taken into consideration in data analysis.

Description of Actual Data Sample:

Initial N: 2128 women with a completed prenatal dietary questionnaire and current enrollment in the research project.

Attrition (final N): 341 mother/child pairs

Age: 32.6 years with a standard deviation of 4.7 years

Ethnicity: 82% white, 9% other, 6% black and 2% Hispanic

Other relevant demographics: well educated group, 96% married or living with partner, most women were nonsmokers

Anthropometrics

Location: Boston, Massachusetts

Summary of Results:

Key Findings

- Mean maternal fish intake varied from 0 to 7.5 servings; the mean intake was 1.5 servings with a standard deviation of 1.4.
- 12% of the mothers consumed fish more than twice per week and 14% of the mothers never consumed fish.
- Mean erythrocyte total mercury score was 3.8 ng/g with a standard deviation of 3.8; 35 mothers were above the 90th percentile.
- Maternal fish intake was directly correlated with erythrocyte total mercury.
- Maternal fish intake (> 2 fish servings per week) compared with no fish intake, the intake was directly associated with higher child WRAVMA scores.
- Maternal DHA + EPA intake from fish was associated with higher PPVT scores and higher WRAVMA scores in the children. Higher maternal erythrocyte mercury levels were associated with worse child test performance.

Other Findings

- Mean child age at testing was 38.4 months and the mean child test scores were 105.7 for the PPVT and 103.2 for the WRAVMA total score.
- Hair mercury was correlated with erythrocyte total mercury and with fish intake
- There was no child cognition advantage if fish consumption was at or below two weekly fish servings, compared with no fish consumption.

Author Conclusion:

Maternal fish intake more than twice a week was associated with improved child performance on tests of language and visual motor skills. Fish consumption of less than or equal to two servings per week was not associated with any benefit. Maternal consumption of fish with lower mercury levels would allow for stronger benefits of fish intake. Recommendations for fish consumption during pregnancy should take into account the nutritional benefits as well as the potential harm from mercury exposure.

Reviewer Comments:

Fish intake, hair mercury and erythrocyte mercury measured. Authors note the following limitations:

- *Unmeasured confounding may account for at least part of the observed findings*
- *Home environment was not assessed*
- *Other neurodevelopmental domains, such as overall intelligence, were not measured*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes

3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes

	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes